REMARKS

The Office Action of March 10, 2004, has been received and reviewed. All claim amendments and cancellations are made without prejudice or disclaimer. The applicants hereby request continued examination and submit the present response under 37 C.F.R. § 1.114.

Claims 19-26, 31 and 33-37 are pending, and claims 17, 18, 27-30, and 32 stand withdrawn. Claims 19, 23-25, 31, and 33-35 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking sufficient written description, and as a consequence, lacking enablement. Claims 19-26, 31, and 33-36 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Claims 19 and 20 stand rejected under 35 U.S.C. § 102(f) as assertedly being the same as the claims 22 and 25 of copending application 09/403,213 and claims 17 and 24 of copending application 09/764,176. Claims 19, 20, and 26 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata *et al.* (PNAS 1998 95:1213-17), in view of Zuckermann *et al.* (U.S. Patent 6,468,986). Claim 37 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata *et al.*, in view of Zuckermann *et al.* and Ledley *et al.* (U.S. Patent 5,792,751). Claims 19-22, 26, and 36 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata *et al.*, in view of Zuckermann *et al.*, McCormick *et al.* (U.S. Patent 5,801,029), and Bujard *et al.*(U.S. Patent 5,814,618). Claims 19 and 20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting. Reconsideration is respectfully requested.

Priority Claim:

In compliance with 35 U.S.C. §§ 119 and 120, the application has been amended to reference the priority claim established in the PCT application. Reconsideration is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph:

Claims 19, 23-25, 31, and 33-35 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking sufficient written description, and as a consequence, lacking enablement.

Support for gene delivery vehicles having a tropism for specific cells is described in the specification, for example, page 4, lines 13-20, the paragraph spanning pages 4-5, and page 8, lines 26-34. Moreover, "a patent specification is not intended nor required to be a production specification" In re Gay, 309 F.2d 768, 135 USPQ 311 (CCPA 1962). Therefore, since the means for obtaining the desired tropism are known in the art, the specification provides the necessary description and guidance of such tropism determinants. Thus, the specification provides a sufficient written description and enables a person of ordinary skill in the art to make and use the invention.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph:

Claims 19-26, 31, and 33-36 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Specifically, "the apoptosis inducing protein" has been amended to "an apoptosis inducing protein" to correct the antecedent basis. Therefore, the amendment should overcome the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection under 35 U.S.C. § 102(f):

Claims 19 and 20 stand rejected under 35 U.S.C. § 102(f) as assertedly being the same as the claims 22 and 25 of copending application 09/403,213 and claims 17 and 24 of copending application 09/764,176.

The applicants note that even beyond the relative filing dates, application number 09/403,213 is the same inventive entity as the present invention, the inventors of both are Mathieu Hubertus Maria Noteborn and Alexandra Maria Pietersen and both are assigneed to Leadd B.V. Thus, the 09/403,213 application is not by another and does not qualify as a § 102(f) reference.

With regard to application number 09/764,176, Dr. Noteborn is also an inventor named on that application as well and both are assigned to Leadd. The fact that the inventors are not

identical represents the difference in the applications and claims. However, Dr. Noteborn is a named inventor on all of the applications at issue. Therefore, the inventorship of the present application is correct in that the 09/764,176 application discloses subject matter invented by the applicant rather than derived from the author (MPEP §2137.01).

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejections under 35 U.S.C. § 103(a):

Claims 19, 20, and 26 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata *et al.* (PNAS 1998 95:1213-17), in view of Zuckermann *et al.* (U.S. Patent 6,468,986).

The applicants thank the Examiner for the explanation of how the references are believed to combine and disclose the claimed invention. However, the FasL-Fas system of Sata *et al.* and the general disclosure of apoptotic agents (pro-apoptotic agents) do not teach or suggest the use of apoptin, which has the unique property that it does not induce apoptosis in healthy cells. Thus, there are a specific set of requirements that must be present in a cell before apoptin will induce apoptosis (for example, *see*, page 7, lines 4-22, and page 10, lines 16-26 of the specification). Neither Sata *et al.* nor Zuckermann *et al.*, either alone or in combination, teach or suggest that cells of in an inflammatory disorder or an immune disease have the requisite requirements. In the absence of such a teaching, a person of ordinary skill in the art would not be motivated to combine the references and to treat an inflammatory disease or an immune disease. In particular, the unique properties of apoptin do not make it a "generic alternative to FasL." Therefore, the references, either alone or in combination, do not teach or suggest the use of apoptin for the treatment of an inflammatory disorder or an immune disease.

In addition, a person of ordinary skill in the art would be disinclined to use apoptin, which is specific to transformed or at least stressed cells, for the treatment of an inflammatory disease or an immune disease. Furthermore, the properties of apoptin and the required cellular conditions do not produce a situation wherein a person of ordinary skill in the art would have a reasonable expectation of success.

Reconsideration and withdrawal of the rejection are respectfully requested.

Claim 37 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata *et al.*, in view of Zuckermann *et al.* and Ledley *et al.* (U.S. Patent 5,792,751). The Office asserts that Sata *et al.* and Zuckermann *et al.* teach administering to aberrant cells of the subject a recombinant adenoviral vector encoding apoptin and that Ledley *et al.* teaches using gene therapy for treating diseases associated with fluid spaces such as synoviocytes. For the sake of argument, even assuming this to true, Ledley *et al.* do not teach or suggest administering apoptin to treat synoviocytes. The most that can be said is that Ledley *et al.* has a generic statement to the effect that apoptotic genes could be used, but does not teach or suggest that synoviocytes in rheumatoid arthritis have the necessary properties to induce the apoptotic properties of apoptin. In particular, apoptin does not induce apoptosis in normal cells, but does induce apoptosis in transformed cells (*see* page 7, lines 4-22 of the specification). Since the synoviocytes of rheumatoid arthritis are not known to have the properties of transformed cells, a person of ordinary skill in the art would not be motivated to use apoptin to treat such cells, absent the showing in the present application that such cells do in fact possess the required attributes for treatment with apoptin (*see* page 16, lines 25-32 and page 17, lines 14-18 of the specification).

Moreover, Ledley *et al.* teaches away from using adenoviral vectors. Specifically, Ledley *et al.* state that "such vectors [adenoviral vectors] are specifically **unsuitable** for gene therapy of disorders such as arthritis ..." (col. 5, lines 58-60 of Ledley *et al.*). Because Ledley *et al.* teaches away from the use of an adenoviral vector, there is no motivation to combine the adenoviral vector of Sata *et al.* and the apoptotic agents of Zuckermann *et al.* with Ledley *et al.* Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 19-22, 26, and 36 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Sata *et al.*, in view of Zuckermann *et al.*, McCormick *et al.* (U.S. Patent 5,801,029), and Bujard *et al.*(U.S. Patent 5,814,618).

As discussed above in regard to Sata *et al.* and Zuckermann *et al.*, these references do not

teach or suggest that inflammatory response cells have the requisite conditions necessary to stimulate apoptin induction of apoptosis. Furthermore, neither McCormick *et al.* nor Bujard *et al.* teach or suggest that inflammatory or the cells of an immune disease would be susceptible to treatment with apoptin. Therefore, the references, either alone or in combination, do not teach or suggest the use of apoptin for the treatment of an inflammatory disorder or an immune disease.

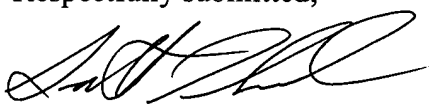
Double patenting rejection:

The applicants will address the double patenting rejection at such time as allowable subject matter is identified and recognize that the Office will maintain the rejection until it is addressed, either by claim amendment or the filing of a terminal disclaimer.

CONCLUSION

If questions remain after entry of the amendments and consideration of the remarks, the Office is kindly invited to contact the applicants' representative at the number provided herein.

Respectfully submitted,



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